

## DRAWINGS ATTACHED

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 3S7F 3S7K

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## (54) MICRO-ADSORPTION DETECTORS

(71) We, VARIAN ASSOCIATES, a corporation organised and existing under the laws of the State of California, United States of America, of 611 Hansen Way, Palo Alto, California, United States of America, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

This invention relates to micro-adsorption detector apparatus.

According to the present invention there is provided a micro-adsorption detector apparatus comprising at least three detector cells serially disposed in close proximity to each other along a flow path for a fluid stream to be detected so as to be traversed in succession by said fluid stream, at least one of said cells holding therein a packing material which material is adsorptively active for a constituent of said fluid stream, and each of said cells including a thermally responsive sensing element for deriving an electrical output which in the case of the said one cell is, in operation, determinative of the adsorption in the respective cell of the said constituent of the fluid stream.

Examples of embodiments of the invention will be described hereinafter with reference to the accompanying drawings.

Heretofore, micro-adsorption detector cells have been serially arranged in the flow path of the output of a liquid chromatographic column for detecting the output peaks. Such a detector is described in the Journal of Gas Chromatography, page 197, April 1967. While such a detector has numerous advantages for use in liquid chromatography (LC), it has one disadvantage. This disadvantage is that the detector is relatively sensitive to changes in the rate of fluid flow. This flow sensitivity precludes the use of the detector with pulsating-type pumps and translates a long term change in fluid flow rate into an annoying baseline drift. The reason for the

flow sensitivity is that the heat dissipated in the upstream thermistor is carried downstream to the second thermistor. The amount of heat carried to the downstream thermistor is a function of the flow rate.

Therefore, it is desirable to provide a micro-adsorption detector the output of which is relatively independent of the flow rate so that the detector may be used with conventional pulsating pumps. It is also desired that the micro-adsorption detector be made more specific and more qualitative as regards the detection of certain sample constituents.

In the accompanying drawings:

Fig. 1 is a schematic line diagram, partly in block diagram form, of a chromatograph according to the present invention,

Fig. 2 is a schematic circuit diagram of a known micro-adsorption detector,

Fig. 3 is a schematic circuit diagram of a micro-adsorption detector according to the present invention,

Fig. 4 is a schematic block diagram of a comparator employed for comparing the outputs of the circuit of Fig. 3,

Fig. 5 is a schematic drawing, partly in block diagram form, of a recorder for comparing the outputs of the circuit of Fig. 3,

Fig. 6 is a schematic diagram of an alternative embodiment of a detector according to the present invention,

Fig. 7 is a schematic circuit diagram of a micro-adsorptive detector according to the present invention,

Fig. 8 is a plot of detected output signal amplitude versus flow rate for an empty detector and for a packed detector, each detector being at a different level of bridge voltage,

Fig. 9 is a circuit similar to that of Fig. 7 depicting an alternative embodiment of the present invention for eliminating flow sensitivity,

Fig. 10 is a schematic block diagram of a circuit for comparing the outputs of the circuit of Fig. 9,

[Price 25p]

Fig. 11 is a schematic circuit diagram for an alternative detector circuit to that of Fig. 9, and

Fig. 12 is a longitudinal sectional view of a micro-adsorptive detector according to the present invention.

Referring now to Fig. 1, a micro-adsorption detector 1 includes three detector cells  $S_1$ ,  $S_2$  and R serially arranged in close proximity to each other along the flow path of a fluid stream 2. The fluid stream may either be a gas or a liquid. In a preferred embodiment the adsorption detector 1 is employed for analysing the effluent stream of a liquid chromatographic column 3 into which a sample to be analysed is injected, as indicated at 4. The output of the chromatographic column 3 comprises a time separation of sample constituents in a solvent stream. As the sample stream 2 passes through the detector 1 the sample peaks are sequentially adsorbed and sometimes desorbed from the packing material 5, if any, positioned within each of the detector cells  $S_1$ ,  $S_2$  and R. The fill material 5 is held within each of the cells by means of suitable fluid-permeable walls, such as filter paper membranes 6.

The micro-adsorption detector 1 makes use of the same physical effect which is used in separation by elution chromatograph, i.e. the different affinities of the eluent and the eluted substance for the stationary phase. Thus, the method is equally valid when the eluent is gaseous or liquid, the stationary phase solid or liquid. With each sequential step of adsorption and desorption in the various cells of the detector 1, there is associated both an evolution and an uptake of heat whose values are equal but of opposite sign. The heats of adsorption and desorption are proportional to the concentration of the substance in the stationary phase. A change in the concentration of the substance in the eluent will, therefore, cause a change of temperature, provided the eluted substance and the eluent have differing affinities for the stationary phase. Thus, there is a rise in temperature in each of the cells when the maximum of a peak in the output of the chromatographic column reaches the particular cell. The following fall in temperature would generally be equal to the preceding rise in temperature, except that there is a loss of heat to the immediate surroundings. Therefore, as the front of a peak passes a given point, a certain amount of the heat evolved will be transported away so that the temperature expected under adiabatic conditions will not be reached. On the passage of the end of the peak, this heat dissipates and the temperature will sink below the ideal starting temperature. The original temperature will once again be obtained by conduction from the surroundings. Typical changes in temperature are shown by the signal traces of Figure 5.

Each of the detector cells  $S_1$ ,  $S_2$  and R includes a thermistor sensing element 7 for sensing the change in temperature of the cell with adsorption and desorption. The known electrical circuit for connection of the thermistors of the sample  $S_1$  and reference cells R, respectively, is shown in Figure 2. Briefly, the thermistor of the sample cell  $S_1$  and the thermistor of the reference cell R were connected in first and second arms, respectively, on the same side of a Wheatstone's bridge 12. Reference resistors 13 and 14 were connected in the remaining two arms of the bridge, on the opposite side thereof, for balancing the bridge, in the absence of a signal to be detected. The reference cell was filled with an inert packing material 5 such as glass beads, whereas the sample cell  $S_1$  was filled with a relatively active adsorptive material.

The bridge was energized from a constant voltage supply 15 and the changes of temperature of the sample or sensing cell  $S_1$ , relative to the reference cell R, were sensed by thermistors 7 and resulted in an unbalance of the bridge, producing an electrical output signal  $E$ . The output signal had the characteristic shape as shown by either of the signal traces depicted in Figure 5.

The problem with this known arrangement is that it yields quantitative information but very little qualitative information. Often times the output signal would have a plurality of relatively closely spaced peaks and it would be desirable to differentiate the different sample constituents within the one composite peak.

Therefore, the adsorption detector 1, according to the present invention, was constructed to include a second sensing cell  $S_2$ , employing a different adsorptive fill material 5 from that employed in the first sensing cell  $S_1$ . It is quite unlikely that two different sample constituents will have the same adsorptive characteristics for two different adsorptive materials, especially when the materials are selected to provide different adsorptive characteristics; for example, one of the adsorptive fill materials could be an ion exchange resin, whereas the other adsorptive material in the second sensing cell could be a surface adsorptive material. Alternatively, a polar surface adsorptive fill material may be used in one cell and a non-polar surface adsorptive material used in the second cell. A comparison of the adsorptive characteristics of the sample on the two different adsorptive materials will yield qualitative results not obtainable by use of a single adsorptive fill material.

Referring now to Figure 3, there is shown a bridge network for use with the adsorptive detector 1 of Figure 1. The circuit is essentially the same as that of Figure 2 with the exception that it includes a second bridge network 16 connected in parallel with the

first bridge 12. The second bridge network 16 includes the thermistor (not shown) of the second sensing cell  $S_2$  connected in one side of the Wheatstone bridge 16 with the thermistor (not shown) of the reference cell R. The other side of the Wheatstone's bridge 16 includes balancing resistors 13' and 14'. The output signal  $E_2$  of the second bridge 16 is taken across the diagonal thereof, in the conventional manner.

A switching network 17 is provided for sequentially switching the thermistor of the reference cell R into circuit in alternate ones of the bridges 12 and 16, at a relatively rapid rate. Although mechanically ganged switches 18 are shown, for the sake of explanation, it is to be understood that any conventional switching arrangement may be employed, such as commutators, gating diodes, and the like, in place of the mechanical switches 18. Also, a stage of synchronous detection referenced to the switching rate is preferably employed for detecting the output signals of the bridges 12 and 16 in such a manner that the pulsating effect of the switching on the output signals  $E_1$  and  $E_2$  can be eliminated. The synchronously detected output signals  $E_1$ ,  $E_2$  are then fed to a comparator 19 as shown in Figure 4. The output of the comparator is an output signal determinative of the difference between the two output signals  $E_1$  and  $E_2$ . Alternatively, the two synchronously detected output signals  $E_1$  and  $E_2$  may be fed to galvanometer recorders 21 and 22 (Figure 5) for recording their respective output signals on the same time scale on a strip chart recorder for visual comparison.

Comparison of the adsorptive characteristics of different sample constituents and different adsorptive material may be used to advantage in several ways. More particularly, the two active cells  $S_1$  and  $S_2$  can be filled with different types of adsorbent, as previously referred to. It would be fortuitous if two different adsorbent materials gave the same relative response for chemically different compounds. Comparison of the output signals  $E_1$  and  $E_2$  from the two cells  $S_1$  and  $S_2$  provides qualitative information on the chemical identity of the sample material. Furthermore, one particular adsorbent may give a better response for many of the compounds in a sample, while another adsorbent gives a better response for the remaining compounds. An investigator, offered the additional degree of freedom of the second adsorbent, should be able to optimize his system for maximum response.

Moreover, overlapping micro-adsorption detector peaks may be difficult to evaluate. By the use of selective adsorbent materials in cells  $S_1$  and  $S_2$ , such adsorbents having characteristics which complement each other, it is possible to achieve a greater separation between peaks. In an ideal case, alternate

peaks would occur on each of the two chromatograms as schematically indicated by the signal traces in Figure 5.

One additional use for the adsorption detector employing two sample cells  $S_1$  and  $S_2$  is for measuring relative strengths of adsorption of different sample-solvent sorbent combinations for use in chromatographic columns. Thus, valuable information regarding suitable combinations for packing various chromatographic columns may be obtained. The strength of adsorption of a column-packing material in one cell  $S_1$  is comparable directly to a standard absorbent in the other cell  $S_2$ . Or the relative strengths of adsorption for two materials of interest are comparable directly.

Referring now to Figure 6, the detector 25 is identical to the detector 1 of Figure 1 with the exception that an additional reference cell  $R_2$  has been added in the flow path in series with the other cells  $S_1$ ,  $R_1$  and  $S_2$ . The detector 25 would be used in a bridge network of the type shown in Figure 7. The bridge network of Figure 7 is substantially the same as that previously described with reference to Figure 3 with the exception that the second reference cell  $R_2$  is placed in the second bridge 16 and the first reference cell  $R_1$  is placed in the arm 11 of the first bridge. The switching arrangement for switching the reference sample between the two bridges is thereby eliminated. The second reference cell  $R_2$  may be packed with an inert or relatively inactive absorbent fill material, such as glass beads, or it may be left empty. The two bridges 12 and 16 are balanced for the pairs of sensing and reference cells  $S_1$  and  $R_1$  and  $S_2$  and  $R_2$ , respectively, in the absence of a sample constituent to be detected.

In operation, heat exchange of the sample constituents on the adsorbent in the sensing cells  $S_1$  and  $S_2$  produces output signals  $E_1$  and  $E_2$ , respectively, which may then be compared in the comparators of Figures 4 or 5, as desired. The detector 25, the bridge circuit of Figure 7 and the comparators of Figures 4 and 5 may be used in precisely the same manner as previously described with reference to the three-cell detector 1. The advantage of the four-cell detector 25 is that the switching and synchronous detection features may be eliminated by the more addition of one additional reference cell  $R_2$ .

Referring now to Figure 8, there is shown a plot of recorder chart scale deflection,  $-A$ , versus flow rate in cc's per hour of the flow stream for two conditions of bridge voltage and two conditions for the pairs of detector cells (S-R pairs), namely, packed or empty. The curves of Figure 8 indicate the fluctuations in background signal as a function of the flow rate. Thus, it is seen that a pulsating flow stream, such as that obtained by use of pulsating pump, would introduce

serious noise in the output signal. Therefore, it is desired to obtain means for compensating for the dependence of the output signal upon the flow rate of the stream to be detected.

5 An interesting characteristic of the curves of Figure 8 is that the flow rate dependence of the output signal from a pair of packed cells, i.e., ones packed with adsorbent or with an inert material, is substantially the same as that from a pair of empty cells. Furthermore, it can be shown that the magnitude of the above-described effect is, to the first order, proportional to the bridge voltage. Accordingly, by changing the bridge voltage the two curves can be brought into coincidence.

Referring now to Figure 9, there is shown a bridge network 26 for compensating for changes in that the output signal due to changes in the flow rate. More particularly, the bridge network 26 of Figure 9 is substantially identical to that previously described with reference to Figure 7 except that the second sensing or sample cell  $S_2$  in the bridge 16 has been replaced by a reference cell  $R_1$  which is placed in the flow and may be either an unpacked sensing cell  $S_2$  or such a sensing cell  $S_2$  packed with an inert packing material. In addition, a pair of variable resistors 27 and 28 have been provided for adjusting the voltages applied to the bridges 12 and 16, respectively.

The two output signals  $E_1$  and  $E_2$  from the bridge 26 are fed to a comparator or subtractor circuit 29, as shown in Figure 10. In the subtractor circuit, the two input signals  $E_1$  and  $E_2$  are subtracted to obtain the output signal  $E_0$  which is thereby corrected for flow rate fluctuations. If necessary, the resistors 27 and 28 are adjusted to bring the flow rate characteristic curves into coincidence, as previously described with reference to Figure 8. In this manner, the output signal  $E_0$  is substantially completely corrected for fluctuations in flow rate and this permits a pulsating type pump to be utilized for producing the flow in the sample stream 2.

Referring now to Figure 11, there is shown an alternative bridge network 31 to that previously described with reference to Figures 9 and 10. In this embodiment, the reference cells  $R_1$  and  $R_2$  are placed in the two arms of the bridge on the opposite side of the bridge to the arms 9 and 11 which contain the detector cells  $S_1$  and  $R_1$ . The output signal  $E_0$  is thereby compensated for fluctuations in flow rate and the only signal appearing at the output  $E_0$  would be due to the heat exchange conditions occurring within the sensing or sample cell  $S_1$ .

60 In all the bridge circuits described, except for that of Fig. 11, individual output signals from the cells are combined in pairs to form at least two separate composite output signals.

In the Fig. 11 configuration, at the balanced condition, the bridge automatically takes the difference of appropriate pairs and then the difference between these two pairs. For example, the output signal from the first sensing cell  $S_1$  is combined with the output signal of the reference cell  $R_1$  to produce in the diagonal of the bridge a composite signal which is relatively insensitive to changes in the ambient temperature, since ambient changes influence the two detectors in the same way. In other words, the combined output signal changes only when the thermal conditions in one of the cells changes relative to the thermal conditions in the other cell. Likewise, the second sensing cell  $S_2$  has its output combined with the output signal from the reference cell  $R_2$  or, in the case of the four-cell detector, with that from the second reference  $R_2$ , to produce a second composite signal in the diagonal arm of the bridge. These two composite output signals may then be compared, for example, by a comparator which gives only the difference between the two or by simultaneously recording the two composite signals for visual comparison, as shown in Figure 5.

Referring now to Figure 12, there is shown, in longitudinal section, a four-cell micro-adsorption detector 25 of the type schematically indicated in Figure 6. The detector includes a pair of stainless steel disc-shaped flanges 35 having a central bore 36 therein to define a portion of the flow passageway for flow of the fluid stream 2 through the detector 25. A plurality of "Teflon" (Registered Trade Mark) discs 37 are centrally apertured at 38 and axially stacked in the space intermediate the flanges 35 to define the main body of the detector 25. A thermistor 7 is centrally mounted in each of the discs 37 with the thermistor element projecting into the flow stream 2. The filter membranes 6 separate the discs 37 to define the boundaries of each of the detector cells. Suitable packing material is placed within the cells defined by the spaces between the filter membranes 6. A metallic centre disc 41, for example of stainless steel, is placed midway in the stack of the "Teflon" discs 37 for separating the two upstream detector discs 37 from the two downstream detector discs 37. The central passage in the centre disc is constricted relative to the passageways through the "Teflon" discs 37 so that heat evolved into the flow stream 2 by the thermistor detectors in the upstream portion of the detector is absorbed by the centre disc to render the downstream detectors relatively insensitive to flow rate conditions produced by the upstream detectors. This feature of the metallic heat-absorbing disc between a pair of micro-adsorption cells is described in the specification of United States Patent No. 3,535,918.

## WHAT WE CLAIM IS:—

1. A micro-adsorption detector apparatus comprising at least three detector cells serially disposed in close proximity to each other along a flow path for a fluid stream to be detected so as to be traversed in succession by said fluid stream, at least one of said cells holding therein a packing material which material is absorptively active for a constituent of said fluid stream, and each of said cells including a thermally responsive sensing element for deriving an electrical output which in the case of the said one cell is, in operation, determinative of the adsorption in the respective cell of the said constituent of the fluid stream.

2. Apparatus according to claim 1, wherein at least two of said cells includes a packing material which is adsorptively active for a constituent of the fluid stream relative to the adsorptive characteristics of the packing material, if any of a third cell.

3. Apparatus according to claim 1, wherein at least two of said cells each includes either no adsorptive packing material or one which is relatively inert as compared to a relatively active fill material disposed within a third cell.

4. Apparatus according to any preceding claim, including means for combining the individual outputs of said sensing elements to form two separate composite output signals each comprising a combination of the outputs of at least two of said cells, and means for comparing the composite output signals.

5. Apparatus according to claim 4, wherein said comparing means includes a recorder for recording the separate composite signals for comparison.

6. Apparatus according to claim 4, wherein said combining means includes a bridge network having said sensing elements disposed in different arms thereof.

7. Apparatus according to claim 4, wherein said combining means includes a pair of Wheatstone's bridge networks, and wherein said comparing means compares the separate outputs of said networks.

8. Apparatus according to claim 1, wherein at least three of said detector cells each includes either no adsorptive fill material or one which is relatively inert as compared to a relatively active fill material disposed within a fourth cell, there being provided means for combining the outputs of two pairs of said sensing elements to produce a pair of composite outputs, and means for comparing the composite outputs to derive an output which is substantially independent of the rate of flow of said stream.

9. Apparatus according to any preceding claim arranged to detect the effluent liquid stream of a chromatographic column disposed upstream of said detector cells.

10. Micro-adsorption detector apparatus substantially as hereinbefore described with reference to Figure 1, or Figure 3, or Figures 3 and 4, or Figures 3 and 5, or Figure 6, or Figure 7, or Figure 9, or Figures 9 and 10, or Figure 11, or Figure 12 of the accompanying drawings.

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London, E.C.4.

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Published by The Patent Office, 25 Southampton Buildings, London, WC2A 1AY, from  
which copies may be obtained.

FIG. 1

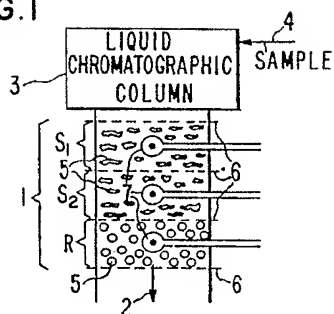


FIG. 2  
PRIOR ART

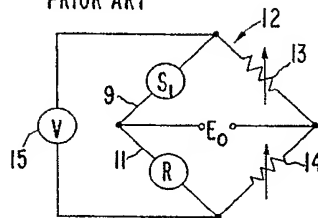


FIG. 3

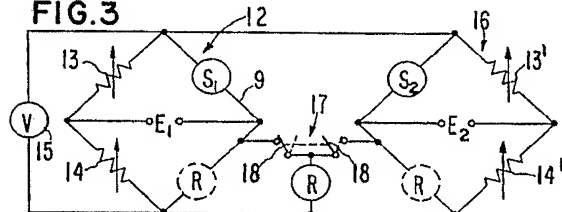


FIG. 4

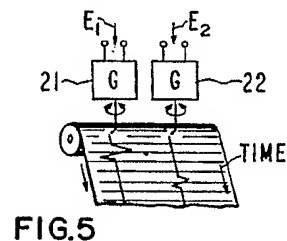
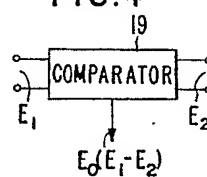


FIG. 5

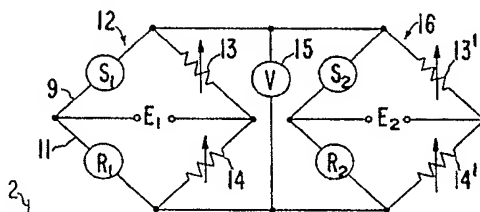
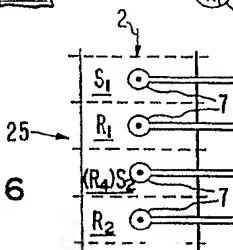
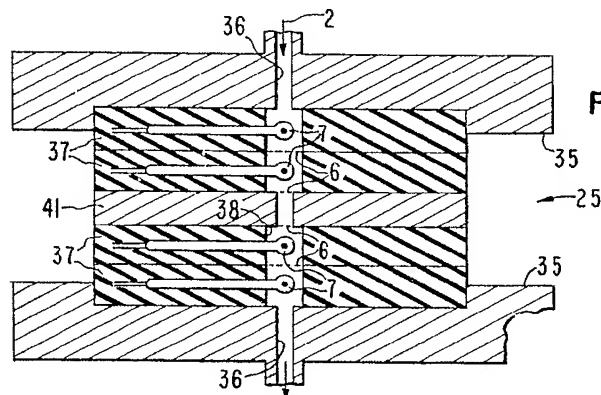
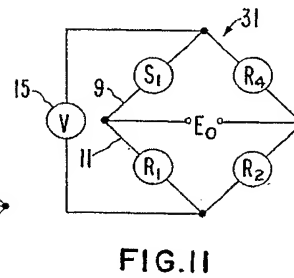
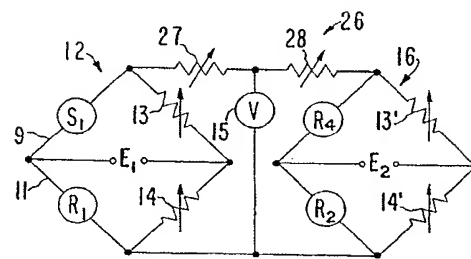
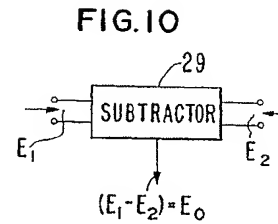
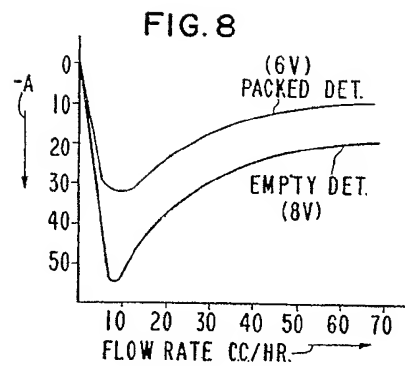


FIG. 7

FIG. 6





## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US01/29137

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : G01N 15/06, 21/64; 30/00, 35/08; B01D 11/00

US CL : 422/55, 57, 69, 81; 436/34, 52, 172; 210/634

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 422/55, 57, 69, 81; 436/34, 52, 172; 210/634

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
CAS Online, East

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5,716,852 A (YAGER et al.) 10 February 1998 (10.02.1998), Abstract and figure 1.	1-2, 4, 7, and 22
X	US 5,932,100 A (YAGER et al.) 03 August 1999 (03.08.1999), Abstract and figure 2, 4, and 6.	1 and 22
—		-----
Y		3-5, 10, and 11
X	US 5,972,710 A (WEIGL et al.) 26 October 1999 (26.10.1999), column 18, lines 47-57, figure 7a, column 19, lines 7-45, figure 8, and figure 9c.	1-11
X	US 5,971,158 A (YAGER et al.) 26 October 1999 (26.10.1999), column 17, line 15-36, and figure 9.	1 and 22
—		-----
Y		2-9, and 11
X	WO 97/00442 A1 (UNIVERSITY OF WASHINGTON) 03 January 1997 (03.01.1997), Abstract, and figure 6.	1 and 22



Further documents are listed in the continuation of Box C.



See patent family annex.

## \* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"B" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T"

Inter document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X"

document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y"

document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&amp;"

document member of the same patent family

Date of the actual completion of the international search

19 November 2001 (19.11.2001)

Date of mailing of the international search report

13 February 2002 (13.02.02)

Name and mailing address of the ISA/US

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Long V. Le

Telephone No. 703-308-0196



# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US01/29137

## Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
  
2. ☐ Claim Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
  
3. ☐ Claim Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:  
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☒ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.: 1-11 and 22
  
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest ☐ The additional search fees were accompanied by the applicant's protest.  
☐ No protest accompanied the payment of additional search fees.

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US01/29137

### BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claims 1-11, drawn to an apparatus with two inlets.

Group II, a claim 12-17, drawn to an apparatus with microfluidic diffusion channel having first and second ends.

Group III, claims 18-21, drawn to a sample analysis instrument for use with a cartridge.

Group IV, claim 22, drawn to an apparatus with two or more streams in laminar flow.

Group V, claims 23-32, drawn to a method for enhancing detection of a diffusion pattern.

The inventions listed as Groups I-V do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: the special technical feature of Group I invention is the specific inlets claimed therein. The special technical feature of Group II invention is the specific a microfluidic transforming turn channel attached to second end of a diffusion channel and the first end of a detection channel claimed therein. The special technical feature of Group III invention is the specific a cartridge claimed therein.

The special technical feature of Group IV invention is the specific a laminar flow having a narrow interface claimed therein. The special technical feature of Group V invention is the specific method of increasing the dimension of streams claimed therein. Since the special technical feature of Group I invention is not present in Group II-V claims and the special technical feature of Group II-V inventions is not present in the Group I claims, unity of invention is lacking. Since the special technical feature of Group II invention is not present in Group III-V claims and the special technical feature of Group III-V inventions is not present in the Group II claims, unity of invention is lacking. Since the special technical feature of Group III invention is not present in Group IV-V claims and the special technical feature of Group IV-V inventions is not present in the Group III claims, unity of invention is lacking. Since the special technical feature of Group IV invention is not present in Group V claims and the special technical feature of Group V inventions is not present in the Group IV claims, unity of invention is lacking.

It is noted that claims 24-30 incorrectly depend upon method of claim 22. Claim 22 is an apparatus claim. Claim 23 is the method claim from which claims 24-30 apparently depend and accordingly claims 24-30 are placed in group V with claim 23. Similarly, claim 32 should depend on claim 31 in view of the term "change."